REMARKS

Claims 1, 3, and 5-16 were pending. Claims 10-12 are withdrawn as directed to a non-elected invention. Claims 1, 3, 5-9 and 13-16 stand rejected.

Support for the amendments is found at p. 7, ll. 31-32, at p. 8, ll. 9-13, and elsewhere in the specification. No new matter is added.

Rejections under 35 U.S.C. § 112

Item 3. Applicant notes that the rejection under 35 U.S.C. § 112(1) of claims 3-9 is withdrawn.

Rejections under §103.

Item 4. Claim 1 was rejected under §103 as obvious over Meruelo et al., of record.

The Examiner rejects claim 1 on the basis that the claim is drawn to a vaccine comprising a heat inactivated influenza antigen and that Meruelo teaches the use of heat inactivation, of oral administration, and of influenza antigen.

According to Meruelo "Numerous methods of inactivation are presently in use. These include fixation and cross-linking of the virus with formaldehyde or glutaraldehyde, heat inactivation, or inactivation with heavy metal salts such as cesium chloride and others. Nevertheless, there, is still a well-recognized need for improved means of virus inactivation for production of vaccines with greater efficacy, safety and other desirable qualities." Col. 2, ll. 30-37. Meruelo then proceeds to demonstrate the method of inactivating virus with hypericin.

Applicant concurs that inactivating viruses makes perfect sense since no one wants to be vaccinated with a vaccine that contains dangerous, live virus. Note that some vaccines contain live virus (e.g., Sabin's vaccine), but they are all in attenuated or non-pathogenic form. In contrast inactivating viral antigens, i.e., proteins or peptides as in Claim 1 does not make any sense to one skilled in the art. Support for this concept can be found for example in Ooyama's teaching, which expressly calls for avoiding heating antigens above 60 ° C.

Thus, the same process of heating as applied to viruses and antigens has purposes that are diametrically opposed. On one hand, one needs to heat viruses above 60 ° C.

with the goal of killing them, but heating proteins at the temperature above 60 ° C. makes them worthless as antigens due to the well-known phenomenon of denaturation. Meruelo's teaching is directed to killing viruses, however, he fails to teach how heat inactivation may preserve immunogenicity. As there is no evidence in Meruelo's teaching to support preservation of immunogenicity, no one skilled in the art will be motivated to consider his teaching as credible.

The claim as amended is drawn to a vaccine comprising dry and heat-inactivated influenza antigen. Meruelo et al. does not teach a dry and heat-inactivated influenza antigen, as evidenced by a lack of teaching of a method of drying influenza antigen.

Importantly, Meruelo et al. does not teach a dry and heat-inactivated vaccine capable of producing an immune response in a host according to the claim. Rather, Meruelo et al.'s invention is directed to "the process of inactivation of a virus with hypericin and related compounds [that] can preserve and enhance the immunogenicity of the virus." Col. 3, ll. 1-3. There is no description in Meruelo et al. of a dry and heat-treated anti-influenza virus vaccine capable of producing an immune effect in a host when administered orally. All the elements of the claims must be given due weight.

The limitation to dry antigen is appropriate to limit the composition claims because it addresses the content of water and/or other solvent in the antigen.

Withdrawal of the rejection of claim 1 as amended is respectfully requested for at least the reasons provided above.

Item 6. Claims 3-9 and 13-16 stand rejected under §103 as obvious over Meruelo et al. in view of Felici et al. or Ooyama et al., which are of record.

Independent claims 3 and 5 have been amended to specify dry viral pathogen or dry immunogen, respectively.

Felici et al. and Ooyama et al. are relied upon by the Examiner merely to provide support for the concept of making immunogens and compositions in the form of pills. The Examiner does not rely on either Felici et al. or Ooyama et al. to disclose the composition and immunogen of the invention as claimed.

In *Dembiczak,* the court stated: "Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is

rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references." *In re Dembicsak*, 175 F.3d 994, 999 (Fed. Cir. 1999). (Citations omitted.) Furthermore, "[c]ombining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability – the essence of hindsight." *Id.*

The Examiner has not pointed to any motivation in Meruelo et al. to combine with other references. Moreover, there has been no indication of passages in either Felici et al. or Ooyama et al. to suggest a combination with other references to reach the claimed composition, as amended. In the face of a clear lack of motivation to combine the references, there is no prima facie case of obviousness. It is not permissible to pick and choose among references using the present specification and claims as a map. The prior art must have at least a suggestion or expectation as to why combining these references would result in an improved or better functioning composition. Absent such a suggestion one of skill in the art would NOT be tempted to do so. Indeed, combining these references to reach the present claims as amended would be impermissible hindsight guided by the present inventor's specification.

Moreover, Ooyama et al. teaches that it is advantageous to avoid denaturation of the protein antigens. P. 3, ll. 36-37. Indeed, the whole of the Ooyama et al. reference is focused on avoiding degradation of the immunogen by gastric juice. P. 3, ll. 38-39. In consequence, no motivation can exist to combine the teachings of Ooyama et al. and Meruelo et al. because Ooyama et al. teaches away from use of a denatured immunogen, vaccine, or composition for eliciting an immune response.

Furthermore, Felici et al. does not suggest any advantage of a dry and heat-inactivated preparation. On the contrary, Felici et al. states that, *for oral administration of a tablet*, the vaccine or immunogen component can be combined with ethanol, glycerol, water, and the like. Col. 5, ll. 50-53. Thus, Felici et al. also provides reasons not to combine with Meruelo et al.

Thus, for these additional reasons, combination of the references is unwarranted.

Not a single instance of dry and heat-inactivated pathogen or immunogen is taught by the Felici et al. or Ooyama et al. references. In clear distinction, the claims as

amended specify that the composition for eliciting an immune response or immunogen is dry and heat-inactivated.

As stated in Ooyama et al., and known to anyone skilled in the art, oral administration of a protein antigen or immunogen will result in loss of biological activity of the antigen or immunogen due to digestive degradation of the protein in the stomach. *See* Ooyama et al., p. 2, ll. 49-50. ("No vaccine compositions for oral administration has [sic, have] been known so far which are capable of providing vaccine effect efficiently without being affected in the small intestine.") Therefore, Applicant asserts that all prior attempts at creating a vaccine that can retain biological activity upon oral administration were directed at safeguarding the active ingredient of the vaccine against digestive degradation. For example, many vaccines are claimed that have an enteric coating, or gastric acid inhibitors like pH buffers. The Applicant further asserts that not a single example of a human oral vaccine can be found among the multitude of existing vaccines that have shown even the slightest efficacy. The present invention overcomes this belief which has been deeply rooted in the vaccine arts for decades if not centuries. Going against the principal paradigm that has dominated the art of vaccines during the last 200 years constitutes a blatant defiance to everything that has been known before and can be hardly defined as obvious.

Claim 13 is rejected over the combination of Meruelo et al. and either Ooyama et al. or Felici et al. because the latter two references disclose use of magnesium stearate. Claim 13 is non-obvious over the art of record as dependent from a non-obvious claim. Moreover, for the reasons presented above, no motivation exists to combine the references.

Withdrawal of the rejection of claims 3-9 and 13-16 is respectfully requested for at least the reasons presented above.

Conclusion

Entry of the amendment is respectfully requested.

A fee for a Request for Continuing Examination accompanies this Amendment.

A petition for a three month extension of time and fee accompanies this Amendment. If payment of other fees is required to keep the application pending, the

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Director is authorized to debit account no. 22-0185, or to credit the account for any overcharges.

The Examiner is urged to directly contact the undersigned at 202-331-7111, if doing so would speed allowance of the claims.

Sincerely,

Date: October 18, 2006

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